Appl. No. 10/624,044

Amendment dated 27 February 2006

Response filed 26 May 2006

Amendments to the Specification:

Please replace the paragraph at page 1, lines 3-9 with the following corrected paragraph:

This application is a divisional of U.S. Serial No. 09/784,859, filed February 16, 2001, now allowed U.S. Patent No. 6,596,541, which is a continuation-in-part of U.S. Serial No. 09/732,234, filed December 7, 2000, now issued as U.S. Patent No. 6,585,251, which claims the benefit of U.S. Serial No. 60/244,665, filed October 31, 2000, now abandoned, each of which is incorporated by reference herein. Throughout this application various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application.

Please replace the paragraph at page 26, line 23 to page 27, line 14 with the following corrected paragraph:

Prepare miniprep DNA (Sambrook, J., E. F. Fritsch And T. Maniatis. Molecular Cloning: A Laboratory Manual, Second Edition, Vols 1, 2, and 3, 1989; Tillett and Neilan, Biotechniques, 24:568-70, 572, 1998; http://www.qiagen.com/literature/handbooks/plkmini/ plm_399.pdf) of the selected LTVEC and re-transform the miniprep LTVEC DNA into E. coli using electroporation (Sambrook, J., E. F. Fritsch and T. Maniatis, Molecular Cloning: A Laboratory Manual, Second Edition, Vols 1, 2, and 3, 1989). This step is necessary to get rid of the plasmid encoding the recombinogenic proteins that are utilized for the bacterial homologous recombination step (Zhang et al., Nat Genet, 20:123-8, 1998; Narayanan et al., Gene Ther, 6:442-7, 1999). It is useful to get rid of this plasmid (a) because it is a high copy number plasmid and may reduce the yields obtained in the large scale LTVEC preps; (b) to eliminate the possibility of inducing expression of the recombinogenic proteins; and (c) because it may obscure physical mapping of the LTVEC. Before introducing the LTVEC into eukaryotic cells. larger amounts of LTVEC DNA are prepared by standard methodology (http://www.qiagen.com/literature/handbooks/plk/plklow.pdf; Sambrook, J., E. F. Fritsch And T. Maniatis. Molecular Cloning: A Laboratory Manual, Second Edition, Vols 1, 2, and 3, 1989; Tillett and Neilan, Biotechniques, 24:568-70, 572, 1998). However, this step can be bypassed if a bacterial homologous recombination method that utilizes a recombingeenic prophage is used, i.e. where the genes encoding the recombinogenic proteins are integrated into the bacterial chromosome (Yu, et al., Proc Natl Acad Sci U S A, 97:5978-83, 2000), is used.

Appl. No. 10/624,044 Amendment dated 27 February 2006 Response filed 26 May 2006

Please replace the paragraph at page 37, lines 6-15, with the following corrected paragraph: To identify ES cells in which one of the two endogenous mOCR10 genes had been replaced by the modification cassette sequence, DNA from individual ES cell clones was analyzed by quantitative PCR using standard TaqMan® methodology as described (Applied Biosystems, TaqMan® Universal PCR Master Mix, catalog number P/N 4304437; see also http://www.pebiodocs.com/pebiodocs/04304449.pdf). The primers and TaqMan® probes used are as described in Figure 3A-3D. A total of 69 independent ES cells clones where screened and 3 were identified as positive, i.e. as clones in which one of the endogenous mOCR10 coding sequence had been replaced by the modification cassette described above.